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(Translation)

[DOCUMENT NAME] Specification

[TITLE OF THE INVENTION] Method for verifying amount of sample solution, method for controlling measurement system and method for measuring concentration of solution in apparatus for measuring optical characteristic

[CLAIMS]

[Claim 1] A method for verifying an amount of a sample solution comprising the steps of:

(a) detecting at least one selected from the group consisting of a transmitted light component, a scattered light component and a reflected light component of a light by a photosensor while irradiating a sample solution, which is being injected into a sample cell, with said light; and

(b) verifying that a predetermined amount of said sample solution is held in said sample cell based on a change in an output signal from said photosensor.

[Claim 2] The method for verifying an amount of a sample solution in accordance with claim 1,

wherein it is verified that said predetermined amount of said sample solution is held in said sample cell based on the fact that a state, in which an absolute value of an amount of change in said output signal per hour is a first predetermined value or less, has continued for a first predetermined time or longer in the step (b).

[Claim 3] The method for verifying an amount of a sample solution in accordance with claim 2,

wherein an inflow of said sample solution into said sample cell is detected based on the fact that said absolute value has become a second predetermined value or greater, followed by verifying that said predetermined amount of said sample solution is held in said sample cell based on the fact that a state, in which said absolute value of an amount of change in said output signal per hour is the first predetermined value or less, has continued for the first predetermined time or longer, after detecting said inflow in the step (b).

[Claim 4] The method for verifying an amount of a sample solution in accordance with claim 3,

wherein the second predetermined value is greater than the first predetermined value.

[Claim 5] The method for verifying an amount of a sample solution in accordance with claim 1,

wherein a transmitted light component is detected in the step (a), and it is verified that said predetermined amount of said sample solution is held in said sample cell based on the fact that said output signal has become a third predetermined value or greater in the step (b).

[Claim 6] The method for verifying an amount of a sample solution in accordance with claim 1,

wherein a scattered light component is detected in

the step (a), and it is verified that said predetermined amount of said sample solution is held in said sample cell based on the fact that said output signal has become a fourth predetermined value or less in the step (b).

[Claim 7] The method for verifying an amount of a sample solution in accordance with any one of claims 1 to 6, wherein said sample solution is a urine, and a urine discharged in a bowl space of a toilet bowl is injected into said sample cell in the step (a).

[Claim 8] A method for controlling a measurement system comprising a step of:

(c) measuring an optical characteristic of said sample solution, after verifying that a predetermined amount of said sample solution is held in said sample cell with the method for verifying an amount of a sample solution in accordance with any one of claims 1 to 7.

[Claim 9] The method for controlling a measurement system in accordance with claim 8, further comprising a step of:

verifying that said sample solution has become stable based on the fact that a state, in which said absolute value of said amount of change in said output signal per hour is a fifth predetermined value or less, has continued for the second predetermined time or longer, after the step (b) of verifying that a predetermined amount of said sample solution is held in said sample cell, followed by conducting the step

(c) of measuring an optical characteristic of said sample solution.

[Claim 10] The method for controlling a measurement system in accordance with claim 9,

wherein the fifth predetermined value is less than the second predetermined value.

[Claim 11] The method for controlling a measurement system in accordance with any one of claims 8 to 10,

wherein the irradiated light in the step (a) is also used for measuring said optical characteristic in the step (c).

[Claim 12] The method for controlling a measurement system in accordance with any one of claims 8 to 11,

wherein said sample solution is transfused from said sample cell to another sample cell after the step (b), and the rest of the steps are conducted thereafter.

[Claim 13] The method for controlling a measurement system in accordance with any one of claims 8 to 12,

wherein a light, which has been transmitted through said sample solution and further an analyzer, is detected by a photosensor to measure an angle of rotation of said sample solution in the step (c), using said output signal from said photosensor as a transmitted light component.

[Claim 14] The method for controlling a measurement system in accordance with any one of claims 8 to 13, comprising the steps of:

(d) discharging said sample solution from said sample

cell after the step (c); and then

(e) washing said sample cell.

[Claim 15] The method for controlling a measurement system in accordance with claim 14,

wherein the steps (d) and (e) are conducted simultaneously by replacing said sample solution in said sample cell with a cleaning solution.

[Claim 16] The method for controlling a measurement system in accordance with any one of claims 8 to 15,

wherein said sample solution is a urine, the steps (a) to (c) are conducted after said sample cell installed in a position closed to a side wall of a toilet bowl is moved into a bowl space of said toilet bowl, and then the rest of the steps are conducted after said sample cell is restored to the initial position.

[Claim 17] The method for controlling a measurement system in accordance with any one of claims 8 to 16,

wherein said sample solution is a urine, the steps (a) and (b) are conducted after said sample cell installed in a position closed to a side wall of a toilet bowl is moved into a bowl space of said toilet bowl, and the rest of the steps are conducted after said sample cell is restored to the initial position.

[Claim 18] The method for controlling a measurement system in accordance with claim 16 or 17,

wherein a urine and/or a cleaning solution is

discharged into a toilet bowl.

[Claim 19] A method for measuring a concentration of a solution comprising a step of:

measuring an optical characteristic of said sample solution by mixing a predetermined amount of a reagent with said sample solution in the method for controlling a measurement system in accordance with any one of claims 8 to 18, followed by measuring a concentration of a specific substance contained in said sample solution.

[Claim 20] A method for measuring a concentration of a solution comprising a step of:

measuring an angle of rotation of said sample solution to measure a concentration of an optically active substance contained in said sample solution in the method for controlling a measurement system in accordance with any one of claims 8 to 18 and then mixing a reagent with said sample solution, followed by measuring an optical characteristic of said sample solution thereby to measure a concentration of a specific substance contained in said sample solution.

[DETAILED DESCRIPTION OF THE INVENTION]

[0001]

[Technical Field to Which the Invention Belongs]

The present invention relates to a method for verifying an amount of a sample solution, a method for controlling a measurement system and a method for measuring a concentration of a solution used for measuring an optical

characteristic of a liquid sample solution.

They are the methods for verifying that a sample solution is held in a sample cell in an amount required for measurement when it is supplied into the sample cell, and extremely effective particularly when a concentration of the sample solution is measured by injecting a reagent into the sample solution, because it is necessary to fix or control the volume ratio of the sample solution and the reagent.

Further, when the sample solution is a urine, the urine can be directly discharged into the sample cell, and therefore, simplicity and high reliability of urinalysis and compactness and lower price of urinalysis apparatus can be achieved, resulting in high practicability.

[0002]

[Prior Art]

In general, when measuring an optical characteristic of a sample solution, the sample solution is held in a sample cell. This sample cell has such structure that a light propagates through the inside of the sample solution held therein. For example, the sample cell is made of a glass or the like, has the shape of a rectangular solid, and the light-transmitting surface thereof is transparent. In order to measure an optical characteristic of the sample solution, it is necessary to supply a predetermined amount of the sample solution into such a sample cell. Normally, such a sample cell has an opening at the top, through which the

predetermined amount of the sample solution is supplied by a dropper, pipette, syringe or the like.

Further, when measuring a concentration of a specific substance in a sample solution, a predetermined amount of a reagent is mixed with a predetermined amount of the sample solution thereby to fix the volume ratio of the sample solution and the reagent, and then an optical characteristic of an analyte in the sample solution is measured to determine the concentration thereof. It has hitherto been necessary to supply a predetermined amount of a sample solution into the sample cell in order to fix the volume ratio of the sample solution and the reagent, and therefore, there has been required a step of placing the sample solution in a beaker or the like beforehand, and measuring it by a pipette, a syringe or the like to determine the volume, and then supplying the sample solution into the sample cell. This step presents not only a problem of complicating the measurement of a concentration of the sample solution, but also that of making an error due to a mistake during the measuring operation more likely to occur.

Further, when the sample solution is a urine, it is necessary to measure the urine once discharged into a cup or the like, and then supplying it into the sample cell in a predetermined amount. This is troublesome especially when urinalysis is carried out at home and also presents another problem of causing the user to have a great reluctance.



[0003]

[Problem That the Invention Is to Solve]

In view of the above problems in the prior art, it is an object of the present invention to provide a method for verifying that a predetermined amount of a sample solution is held in a sample cell during the sample solution is inflowed into the sample cell. Particularly, when a urine is tested, it is a method for verifying that a predetermined amount of a urine required for a test is held in a sample cell while the urine discharged into a toilet bowl is received by a container or the sample cell itself in a bowl space of the toilet bowl.

According to this method, without previously measuring the amount of the sample solution and supplying it into the sample cell, the mixing ratio of the both can be fixed or controlled by fixing or controlling only an amount of the reagent required for measurement of the sample solution.

Namely, the present invention provides a method for controlling a measurement system that facilitates automation of measurement of a sample solution and enables greater efficiency and labor saving of the measurement and the test, and a method for measuring a concentration of a solution using this.

[0004]

[Means for Solving the Problem]

In order to solve the above problems, the present invention first provides a method for verifying an amount of a

sample solution comprising the steps of: (a) detecting at least one selected from the group consisting of a transmitted light component, a scattered light component and a reflected light component of a light by a photosensor while irradiating a sample solution, which is being injected into a sample cell, with the light; and (b) verifying that a predetermined amount of the sample solution is held in the sample cell based on a change in an output signal from the photosensor. Herein, the inflow of the sample solution may be suspended upon the verification.

Namely, the present invention utilizes the fact that a transmitted light component, scattered light component and reflected light component of the above light change in response to the fact that the surface of the sample solution being injected into the sample cell rises so that the solution surface traverses a fixed optical path of an irradiated light into the sample solution.

In this case, it is effective to verifying that the predetermined amount of the sample solution is held in the sample cell based on the fact that a state, in which an absolute value of an amount of change in the output signal per hour is the first predetermined value or less, has continued for the first predetermined time or longer in the step (b).

[0005]

Also, it is effective to detect an inflow of the sample solution into the sample cell based on the fact that

the absolute value has become a second predetermined value or greater, followed by verifying that the predetermined amount of the sample solution is held in the sample cell based on the fact that a state, in which the absolute value of an amount of change in the output signal per hour is the first predetermined value or less, has continued for the first predetermined time or longer, after detecting the inflow in the step (b).

It is preferable that the second predetermined value is greater than the first predetermined value.

Also, it is effective to detect a transmitted light component in the step (a) and to verify that the predetermined amount of the sample solution is held in the sample cell based on the fact that the output signal has become a third predetermined value or greater in the step (b).

Also, it is effective to detect a scattered light component in the step (a) and to verify that the predetermined amount of the sample solution is held in the sample cell based on the fact that the output signal has become the fourth predetermined value or less in the step (b).

When the sample solution is a urine, it is effective to inject a urine discharged into a bowl space of a toilet bowl into the sample cell in the step (a).

[0006]

Next, the present invention also provides a method for controlling a measurement system comprising the step of:

(c) measuring an optical characteristic of the sample solution, after verifying that a predetermined amount of the sample solution is held in the sample cell with the above-described method for verifying an amount of a sample solution. Herein, after verifying that the predetermined amount of the sample solution is held in the sample cell, the inflow of the sample solution may be suspended.

This method for controlling a measurement system is a method for controlling a measurement system, which is used for a measurement of an optical characteristic, in an optimum condition for the measurement, and it is effective to further verify that the sample solution has become stable based on the fact that a state, in which the absolute value of the amount of change in the output signal per hour is a fifth predetermined value or less, has continued for the second predetermined time or longer, after the step (b) of verifying that a predetermined amount of a sample solution is held in the sample cell, followed by step (c) of measuring an optical characteristic of the sample solution.

It is preferable that the fifth predetermined value is less than the second predetermined value.

Also, it is effective to use the irradiated light in the step (a) for measuring the optical characteristic in the step (c).

Also, the sample solution may be transfused from the sample cell to another sample cell after the step (b), and the

rest of the steps may be conducted thereafter. In this case, the former sample cell is used only for trapping the predetermined amount of the sample solution, and the rest of the steps, such as a measurement of an optical characteristic, are conducted in the latter sample cell.

[0007]

In the above method for controlling a measurement system, a light, which has been transmitted through the sample solution and further an analyzer, can be detected by a photosensor to measure an angle of rotation of the sample solution in the step (c), using the output signal from the photosensor as a transmitted light component.

Also, it is possible to include the steps of: (d) discharging the sample solution from the sample cell after the step (c); and then (e) washing the sample cell.

Also, it is effective that the steps (d) and (e) are conducted simultaneously by replacing the sample solution in the sample cell with a cleaning solution.

Further, it is effective that the sample solution is a urine, the steps (a) to (c) are conducted after the sample cell installed in a position closed to a side wall of a toilet bowl is moved into a bowl space of the toilet bowl, and then the rest of the steps are conducted after the sample cell is restored to the initial position.

Also, it is effective that the sample solution is a urine, the steps (a) and (b) are conducted after the sample

cell installed in a position closed to a side wall of a toilet bowl is moved into a bowl space of the toilet bowl, and then the rest of the steps are conducted after the sample cell is restored to the initial position.

Also, it is preferable that the urine and/or the cleaning solution are discharged into the toilet bowl.

[0008]

Further, the present invention also provides a method for measuring a concentration of a solution comprising a step of measuring an optical characteristic of the sample solution by mixing a predetermined amount of a reagent with the sample solution in the above method for controlling a measurement system, followed by measuring a concentration of a specific substance contained in the sample solution.

Also, it provides a method for measuring a concentration of a solution comprising a step of measuring an angle of rotation of the sample solution to measure a concentration of an optically active substance contained in the sample solution in the above method for controlling a measurement system and then mixing a reagent with the sample solution, followed by measuring an optical characteristic of the sample solution thereby to measure a concentration of a specific substance contained in the sample solution.

[0009]

[Mode for Embodying the Invention]

As discussed above, the present invention relates to

a method for verifying an amount of a sample solution, and a method for controlling a measurement system and method for measuring a concentration of a solution using this. Therefore, the method for verifying an amount of a sample solution in accordance with the present invention will be described first.

As a result of diligent studies on the relation between a level of a sample solution in a sample cell and an optical power propagating through the sample solution by using the apparatus for measuring an optical characteristic shown in FIG. 1, the present inventor has accomplished the method for verifying an amount of a sample solution in accordance with the present invention.

First, such measurement will be described below in detail with reference to FIG. 1. FIG. 1 is a view showing the configuration of an apparatus for measuring an optical characteristic measurement used for carrying out the method of the present invention.

[0010]

In FIG. 1, a skeleton of a sample cell 1 of the present invention is a container made of aluminum which has the shape of a rectangular solid, an opening at the top and a glass plate as an optical window embedded on both ends of the optical path (not shown), so that it allows a light to be transmitted through a sample solution while holding the sample solution therein. The distance from the lowermost part of a surface 2 of the sample solution to the bottom of the sample

cell 1 is indicated with "d". The distance of the long axis of this sample cell, that is, the distance between the optical windows is 50 mm, the distance of the short axis is 10 mm, and the propagating distance in the sample solution is 50 mm. The apparatus for measuring an optical characteristic shown in FIG. 1 comprises a funnel 3 for temporarily trapping the sample solution, an electromagnetic valve 4 for controlling the dropping of the sample solution trapped in the funnel 3 into the sample cell 1, and a pipette 5 for injecting a predetermined amount of a reagent into the sample solution. A semiconductor laser module as a light source 6 projects a substantially parallel light 7, which has the shape of a circle, a wavelength of 670 nm, an intensity of 3.0 mW and a beam radius of 1.0 mm, in a direction perpendicular to the optical windows of the sample cell 1, i.e., in the z direction. This substantially parallel light 7 propagates in a direction parallel to the bottom of the sample cell 1, and the optical axis indicated with the dash-dotted line is located at a height of 8 mm from the bottom. In other words, the center of the circle of the cross section of the substantially parallel light 7 is located at a height of 8 mm from the bottom of the sample cell 1. Then, a photosensor 8 for detecting a light transmitted through the sample solution sends an output signal "S", and a computer 9 analyzes the output signal S from the photosensor 8 to control the electromagnetic valve 4, the pipette 5 and the light source 6.



[0011]

Next, the shape of the cross section of the beam of the substantially parallel light 7 is circular, and the direction of an electric field thereof is indicated with x in FIG. 1. This substantially parallel light 7 is a Gaussian beam, whose optical power density on the optical axis increases to the maximum at the cross section perpendicular to the propagating direction. Then, it decreases with the distance from the optical axis at the cross section of the beam in accordance with the following formula (1):

$$I(r) = I(0) \times \exp(-2r^2/w_0^2) \quad (1)$$

where,  $r$  is a distance (m) from the optical axis at the cross section of the beam;  $I(r)$  is a power density ( $W/m^2$ ) at a distance of  $r$  from the optical axis;  $I(0)$  is a power density ( $W/m^2$ ) on the optical axis; and  $w_0$  is a distance (m) at which the power density is  $1/e^2$  of  $I(0)$ , in which  $e$  is a natural logarithm.

With respect to the beam radius of the substantially parallel light 7 described above, it is defined as; beam radius =  $w_0 = 1.0$  mm. The power included within this beam radius  $r$  is obtained by integrating the power density, and approximately 86.5% of the total power is present within the radius  $w_0$ . Similarly, approximately 99.97% of the total power is present in the  $2 w_0$ , which is two times the beam radius.

Herein, this substantially parallel light 7 is a parallel light in terms of geometrical optics, however, in

actuality, it increases in the beam diameter as it propagates owing to the diffraction effect. However, there is no harm in substantially considering it as a parallel light for the size shown in the present invention.

[0012]

Thus, when the lowermost part of the surface 2 of the sample solution is located at the height two times the beam radius, from the optical axis of the substantially parallel light 7, that is, when  $d = 10$  mm, an optical power that is approximately 99.97% of the total power propagates through the sample solution. At this time, 5 ml or more of the sample solution is held in the sample cell 1.

On the other hand, when the lowermost part of the solution surface 2 is located at a height of 8 mm from the bottom of the sample cell 1, i.e., when  $d = 8$  mm, only an optical power that is about a half of the total power propagates through the sample solution.

The reason why the optical power propagating through the sample solution decreases in such a way when the solution surface 2 is located within the beam of the substantially parallel light 7 is that optical phenomena of reflection, refraction and diffraction concurrently occur on the solution surface thereby to diffuse the beam. For this reason, in the case where the photo detective area of the photosensor 8 perfectly coincides with the cross section of the substantially parallel light 7, when  $d < 10$  mm, the optical

power reaching the photosensor 8 remarkably decreases. That is, in the case where the photo detective area of the photosensor 8 has the shape of a circle having a radius of 1 mm and the center thereof coincides with the optical axis of the substantially parallel light 7, when  $d < 10$  mm, the optical power reaching the photosensor 8 significantly decreases owing to the diffusion of the beam. Furthermore, this diffusion of the beam is greatly influenced by the fluctuation of the solution surface, and thus the optical power reaching the photosensor 8 does not stabilize.

[0013]

Next, the output signal  $S$  from the photosensor 8 was measured when a sample solution was dropped into the sample cell 1 from the funnel 3 at 0.5 ml/sec. using the apparatus for measuring an optical characteristic shown in FIG. 1. The result is shown in FIG. 2. FIG. 2 is a graph showing the relation between the output signal  $S$  from the photosensor 8 and the distance  $d$  from the bottom of the sample cell to the lowermost part of the solution surface. In FIG. 2, the horizontal axis indicates the distance  $d$  from the bottom of the sample cell 1 to the lowermost part of the solution surface, and the vertical axis indicates the output signal  $S$  from the photosensor 8, and  $S$  was adjusted to be 1.0 V when  $d \geq 10$  mm.

Herein, when the sample solution was dropped into the sample cell 1 shown in FIG. 1 at the above dropping rate,  $d$

becomes 1 mm one second after the dropping was started. Therefore, the horizontal axis of FIG. 2 also indicates the elapsed time since the start of the dropping of the sample solution. It should be noted that the sample solution is dropped into the sample cell 1 along the plane thereof without any optical window, so that the sample solution is not present in the optical path of the substantially parallel light 7 during the dropping.

As shown in FIG. 2, no influence of the sample solution is observed until  $d$  becomes approximately 6.0 mm; however, when  $d = 6.0$  to 10 mm, the output signal  $S$  significantly changes under the influence of the diffusion of the beam due to the reflection, refraction or diffraction between the substantially parallel light 7 and the solution surface 2, and furthermore, the fluctuation of the solution surface. Then, when  $d$  is above 10 mm, it apparently stabilizes.

As described above, the present inventor has directed his attention to the fact that the optical power density propagating through the sample solution changes owing to the positional relation between a rising solution surface and the beam axis, and has accomplished the present invention by application of such a change.

[0014]

Namely, the most remarkable feature of the present invention, in the method for verifying an amount of a sample

solution comprising steps of: detecting at least one selected from the group consisting of a transmitted light component, a scattered light component and a reflected light component of a light by a photosensor while irradiating a sample solution, which is being injected into a sample cell, with the light; and verifying that a predetermined amount of the sample solution is held in the sample cell based on a change in an output signal from the photosensor, lies in verifying that the sample solution is inflowing into the sample cell, that a predetermined amount of the sample solution is held in the sample cell, and that a bubble or the like in the sample solution held in the sample cell has disappeared so that it has become stable, by measuring the output signal  $S$  and an absolute value  $|dS(t)/dt|$  of an amount of change in the output signal  $S$  per hour " $t$ ".

Herein, the absolute value  $|dS(t)/dt|$  of the amount of change in the output signal  $S$  per hour  $t$  can be expressed as the gradient of the tangent in the graph shown in FIG. 2. Accordingly, in the present invention, the method for verifying that a predetermined amount of a sample solution is held in the sample cell based on a change in the output signal from the photosensor, for example, on the basis of the test result shown in FIG. 2, can be exemplified by the following combinations. However, it is not limited to these.

[0015]

- (1) An inflow of a sample solution is detected when

$|dS(t)/dt|$  has become a predetermined value (e.g., 0.1 V/sec, which is the absolute value of the gradient of the straight line ab) or greater.

Subsequently, it is verified that a predetermined amount of the sample solution is held based on the fact that  $|dS(t)/dt|$  has become a predetermined value (e.g., 0.01 V/sec) or less and a predetermined time (e.g., 0.5 second from the point c to the point d) or longer has elapsed thereafter.

(2) An inflow of a sample solution is detected when  $|dS(t)/dt|$  has become a predetermined value (e.g., 0.1 V/sec, which is the absolute value of the gradient of the straight line ab) or greater.

Subsequently, it is verified that a predetermined amount of the sample solution is held based on the fact that  $|dS(t)/dt|$  has become a predetermined value (e.g., 0.01 V/sec) or less and S has become a predetermined value (e.g., 0.8 V at the point e) or greater.

(3) An inflow of the sample solution is detected when S has become a predetermined value (e.g., 0.5 V at the point f) or less.

Subsequently, it is verified that a predetermined amount of the sample solution is held based on the fact that  $|dS(t)/dt|$  has become a predetermined value (e.g., 0.01 V) or less and a predetermined time (e.g., 0.5 second from the points c to the point d) or longer has elapsed thereafter.

[0016]

Also, when controlling a measurement system of an optical apparatus by using the above method for verifying an amount of a sample solution, it is preferable to carry out the optical measurement after further measuring  $|dS(t)/dt|$  to verify that a bubble has disappeared or an impurity has sedimented in the sample solution, so that the obstruction to the optical characteristic measurement has been eliminated from the optical path.

Herein, although a predetermined value and a predetermined time referred in this specification vary depending on such conditions as the type and the component of the sample solution, the type of a light to irradiate the sample solution, the type of a light to be detected (a transmitted light component, a scattered light component and/or a reflected light component), they can be set in advance by conducting the above experiment, which was carried out by the present inventor, for the respective types of the sample solutions under a predetermined condition, and preparing a graph showing the relation between the output signal from the photosensor and the distance from the bottom of the sample cell to the lowermost part of the solution surface (or the elapsed time since the start of the dropping of the sample solution) as shown in FIG. 2.

Then, by utilizing such a principle, the present invention also provides a method for controlling a measurement system and a method for measuring a concentration of a sample

solution in the above-described apparatus for measuring an optical characteristic.

[0017]

Particularly, when a urine is used as the sample solution, it is applicable to a method for controlling a measurement system wherein, while the urine discharged into a toilet bowl is received by a sample cell moved into the bowl space and then transfused from the sample cell to another sample cell, the amount of the sample solution held in the former sample cell is verified by using the above method for verifying an amount of a sample solution.

Also, it is applicable to a method for controlling a measurement system wherein the amount of the sample solution held in the sample cell is verified by using the above method for verifying an amount of a sample solution, while the sample cell is moved into a bowl space of the toilet bowl to receive the urine discharged into the toilet bowl in the air.

Further, it is also applicable to a method for verifying an amount of a sample solution and a method for controlling a measurement system wherein, while the urine discharged into the toilet bowl is received in the air by the sample cell moved into the bowl space, a transmitted light component and/or a scattered light component and/or a reflected light component of the light that irradiated the urine in the sample cell are detected by a photosensor to verify that a predetermined amount of the urine is held in the



sample cell based on an output signal from the photosensor, followed by transfusing the urine to another sample cell for holding it to measure an optical characteristic of the urine.

Hereinbelow, the present invention will be further described in detail by way of examples, but the present invention is not limited to these.

[0018]

[Working Examples]

<<Example 1>>

Embodiment 1 of the present invention using the apparatus for measuring an optical characteristic shown in FIG. 1 will be described more concretely.

First, with 5 ml or more of a sample solution being injected in a funnel 3 for trapping, a computer 9 sent an open signal to an electromagnetic valve 4, thereby starting the dropping of the sample solution in the funnel 3 into a sample cell 1 at 0.5 ml/sec.

In the state of sending this open signal, the computer 9 was set to be in a state of being on standby for verifying the amount of the sample solution when an absolute value of an amount of change in an output signal  $S$  from a photosensor 8 per hour  $dS(t)/dt$  had become the second predetermined value or greater. For example, the state of being on standby for verifying the amount of the sample solution was set when the absolute value of the amount of change in the output signal  $S$  per hour  $dS(t)/dt$  had become 0.1

V/sec or greater in FIG. 2.

[0019]

In the state of being on standby for verifying the amount of the sample solution and sending the open signal, it was verified that a predetermined amount of the sample solution was held based on the fact that a state, in which the absolute value of the amount of change in the output signal S from the photosensor 8 per hour  $dS(t)/dt$  was the first predetermined value or less, had continued for the first predetermined time or longer. For example, it was verified that the predetermined amount of the sample solution was held when a state, in which  $dS(t)/dt$  was 0.01 V/sec or less, had continued for 0.5 second or longer, and a close signal was sent to the electromagnetic valve 4. By such a control, d became 10.5 mm or greater, and therefore, 5.25 ml or more of the sample solution was held in the sample cell 1.

Next, in this state, the computer 9 controlled the pipette 5 to inject a predetermined amount of a reagent to be used for measuring a concentration of a specific component in the sample into the sample cell 1, thereby controlling or fixing the volume ratio of the sample solution and the reagent while mixing the both. Then, at this time, the computer 9 analyzed the output signal S from the photosensor 8 to measure the concentration of the specific component in the sample solution.

[0020]

According to this example, not only the amount of change in the output signal  $S$  from the photosensor 8 per hour  $dS(t)/dt$ , but also the duration of this amount of change was verified, and therefore, there was an effect of preventing the following erroneous operation.

Namely, at a point of inflection, at which the output signal  $S$  from the photosensor 8 that had been decreasing turned to increase (or vice versa),  $dS(t)/dt$  reversed in sign of plus and minus. In other words, at this point of inflection which appeared instantaneously during the dropping of the sample solution,  $dS(t)/dt$  became zero. Thus, when it was verified only that the absolute value of  $dS(t)/dt$  had become the first predetermined value or less, there was the possibility that an erroneous operation would occur. This could be also held true from the fact that a plurality of points of inflection were observed in FIG. 2.

In contrast, in the present invention, not only the absolute value of the amount of change in the output signal  $S$  per hour  $dS(t)/dt$ , but also the duration of the amount of change was verified, and therefore, an erroneous operation due to such a plurality of points of inflection could be prevented.

[0021]

As described above, the amount of the sample solution could be verified precisely during the inflow of the sample solution into the sample cell, by setting the state of being on standby for verifying the amount of the sample solution

based on the fact that the amount of change in the output signal per hour  $ds(t)/dt$  had become the second predetermined value or greater, and by verifying that the predetermined amount of the sample solution was held when the stated in which  $S(t)/dt$  was the first predetermined value or less had continued for the first predetermined time or longer.

In this example, since the amount of the sample solution was verified by using the substantially parallel light 7, which was a light for measuring an optical characteristic of the sample solution, and the photosensor 8 for detecting this, it was not necessary to provide any means for verifying the amount of the sample solution separately. In other words, it utilized the original means for measuring an optical characteristic as the means for verifying the amount of the sample solution. Therefore, it was effective and highly practicable. However, it was obvious that the amount of the sample solution could also be verified by providing another substantially parallel light and photosensor aside from the light for measuring an optical characteristic, and operating them in the same manner as in this example.

[0022]

Further, according to this example, the amount of the sample solution held in the sample cell could be verified, so that the volume ratio of the reagent to be injected and the sample solution could be fixed or controlled, without measuring the amount of the sample solution. Consequently,

the steps in the measurement of an optical characteristic of the sample solution could be simplified and an erroneous operation was less likely to occur, resulting in high practicability. That is, according to the present invention, higher efficiency and laborsaving of the measurement and the test became possible.

In this example, the example was shown, in which the substantially parallel light 7 propagated linearly in the z direction and was transmitted through the sample solution thereby to reach the photosensor 8 in FIG. 1; however, when the substantially parallel light 7 was made incident on the optical windows of the sample cell 1 in any angle other than that is perpendicular, and when the respective optical windows of the sample cell were not parallel to each other, the substantially parallel light 7 was refracted before reaching the photosensor 8. Even when the substantially parallel light was refracted on the optical windows or the sample solution in this manner, the amount of the sample solution could be verified by utilizing the same mechanism described in this example, and therefore it is within the technical scope of the present invention.

[0023]

<<Example 2>>

In the following, Example 2 of the present invention will be described in detail in the same manner as in Example 1 with reference to FIGS. 1 and 2. Although the apparatus for

measuring an optical characteristic shown in FIG. 1 was used in this example, the parameter was set differently.

First, with 5 ml or more of a sample solution being injected in the funnel 3 for trapping, the computer 9 sent an open signal to the electromagnetic valve 4, thereby starting the dropping of the sample solution in the funnel 3 into the sample cell 1 at 0.5 ml/sec. In the state of sending this open signal, the computer 9 was set to be in a state of being standby for verifying an amount of a sample solution based on the fact that an absolute value of an amount of change in the output signal S from the photosensor 8 per hour  $dS(t)/dt$  was the second predetermined value or greater. For example, the state of being on standby for verifying the amount of the sample solution was set when the absolute value of the amount of change in the output signal S per hour  $dS(t)/dt$  had become 0.1 V/sec or greater in FIG. 2.

In this state of being on standby for verifying the amount of the sample solution and sending the open signal, it was verified that a predetermined amount of the sample solution was held when the absolute value of the amount of change in the output signal S from the photosensor 8 per hour  $dS(t)/dt$  had become the first predetermined value or less and the magnitude of the output signal S from the photosensor 8 had become the third predetermined value or greater. For example, it was determined and verified that the predetermined amount of the sample solution was held when the absolute value

of the amount of change per hour  $dS(t)/dt$  had become 0.01 V/sec or less and the output signal S had become 0.8 V or greater, and then a close signal was sent to the electromagnetic valve 4. By a control according to such a setting, d became 10 mm or greater, and 5 ml or more of the sample solution was held in the sample cell 1.

[0024]

According to this example, since the amount of the sample solution was verified based on not only the absolute value of the amount of change in the output signal S from the photosensor 8 per hour, but also the fact that the magnitude of the output signal S had become a predetermined value or greater, the following erroneous operation that might occur in this Example 1 could be prevented.

For example, when a bubble adhered to the optical window of the sample cell to be present in the optical path of the substantially parallel light 7 during the inflow of the sample solution into the sample cell, the substantially parallel light 7 was scattered and reflected by this bubble, and therefore could not reach the photosensor 8. In this case, also, the absolute value of the amount of change in the output signal S from the photosensor 8 per hour might become 0.01 V/sec or less, resulting in an erroneous operation of mistakenly verifying that the predetermined amount of the sample solution was held.

Such an erroneous operation due to a bubble, however,

could be prevented by considering the magnitude of the output signal S for the judgment, in addition to the absolute value of the amount of change in the output signal S per hour. Moreover, when the parameter was set as in this example, it was not necessary to verify that the a state, in which absolute value of the amount of change  $dS(t)/dt$  was the second predetermined value or less, continued for the first predetermined time or longer, as compared to the case where it was set as in Example 1, and therefore, it became possible to shorten the time for verifying the amount of the sample solution by the first predetermined time, which was advantageous in increasing the efficiency of the measurement.

As described above, according to this example, the amount of the sample solution held in the sample cell could be verified with high reliability, so that the volume ratio of the reagent to be injected and the sample solution could be fixed or controlled, without measuring the amount of the sample solution. Consequently, the steps could be simplified and an erroneous operation was less likely to occur, resulting in an extremely high practicability of the measurement. Further, according to the present invention, higher efficiency and laborsaving of the measurement and the test became possible.

[0025]

<<Example 3>>

In the following, Example 3 of the present invention



will be described in detail in the same manner as in Example 1 with reference to FIGS. 1, 2 and 3. Although the apparatus for measuring an optical characteristic shown in FIG. 1 was used in this example, the parameter was set differently. Herein, the measurement of an optical characteristic of the sample solution was started from the state, in which the amount of the sample solution held in the sample cell had been verified. Here, FIG. 3 is an enlarged view of FIG. 2 showing the value of the output signal from the photosensor 8 at around 1.0 V, when  $d = 10$  to 12.

First, with 5 ml or more of a sample solution being injected in the funnel 3 for trapping, the computer 9 sent an open signal to the electromagnetic valve 4, thereby starting the dropping of the sample solution in the funnel 3 into the sample cell 1 at 0.5 ml/sec. In this state of sending the open signal, the computer 9 was set to be in a state of being on standby for verifying the amount of the sample solution when the output signal S from the photosensor 8 had become the fifth predetermined value or less. For example, the state of being on standby for verifying the amount of the sample solution was set when the output signal S had become 0.5 V or less in FIG. 2.

In this state of being on standby for verifying the amount of the sample solution and sending the open signal, it was verified that a predetermined amount of the sample solution was held based on the fact that a state, in which the

absolute value of the amount of change in the output signal S from the photosensor 8 per hour  $dS(t)/dt$  was the first predetermined value or less, had continued for a predetermined time or longer. For example, it was verified that the predetermined amount of the sample solution was held when a state, in which  $dS(t)/dt$  was 0.01 V/sec or less, had continued for 0.5 second or longer, and then a close signal was sent to the electromagnetic valve 4. By a control according to such a setting, d became 10.5 mm or greater, and 5.25 ml or more of the sample solution was held in the sample cell 1.

[0026]

Next, from this state, it was verified that a state, in which the amount of change in the output signal S per hour  $dS(t)/dt$  was the fifth predetermined value or less, had continued for the second predetermined time or longer for starting the measurement of an optical characteristic of the sample solution. For example, the point of time, at which a state in which  $dS(t)/dt$  was 0.003 (V/S) or less had continued for 0.5 second or longer, was verified. In FIGS. 2 and 3,  $dS(t)/dt$  had become 0.003 (V/S) or less when 11.1 seconds had elapsed, and therefore, the point of time at which 11.6 seconds had elapsed was verified.

When the above-described point of time was verified, an optical characteristic of the sample solution in the sample cell 1 was measured. For example, the computer 9 controlled the pipette 5 to inject a predetermined amount of a reagent,

which was to be used for measuring a concentration of a specific component contained in the sample solution, into the sample cell 1, thereby fixing or controlling the volume ratio of the sample solution and the reagent. Then, the computer 9 analyzed the output signal S from the photosensor 8 to measure the concentration of the specific component in the sample solution.

[0027]

According to this example, since the amount of change in the output signal S from the photosensor 8 per hour  $ds(t)/dt$  and the duration thereof were verified after verifying that the predetermined amount of the sample solution was held in the sample cell 1, the reliability of the measurement of an optical characteristic could be enhanced because of the following reason.

Even after the inflow of the sample solution into the sample cell 1 was suspended, a bubble or the like generating during the inflow might be present in the optical path of the substantially parallel light 7, thereby causing a fluctuation in the output signal S from the photosensor 8. This fluctuation deteriorated the reliability of the optical characteristic measurement. Therefore, the measurement was started after verifying that the predetermined amount of the sample solution was held and after further verifying that a bubble or the like had disappeared from the optical path, for example, by surfacing, and the fluctuation in the output

signal had subsided by verifying the amount of change  $dS(t)/dt$ . Consequently, the reliability of the measurement could be ensured.

Namely, at a point of inflection, at which the output signal  $S$  from the photosensor 8 that had been decreasing turned to increase (or vice versa),  $dS(t)/dt$  reversed in sign of plus and minus. In other words, at this point of inflection, which generated instantaneously during the dropping of the sample solution,  $dS(t)/dt$  became zero. Thus, when it was verified only that the absolute value of  $dS(t)/dt$  had become the fifth predetermined value or less, an erroneous operation occurred. This could be also held true from the fact that a plurality of points of inflection were observed in FIG. 2.

In contrast, in the present invention, an erroneous operation due to such a plurality of points of inflection could be prevented by verifying not only the absolute value of the amount of change in the output signal  $S$  per hour  $dS(t)/dt$ , but also the duration thereof.

[0028]

According to this example, the amount of the sample solution held in the sample cell could be verified, so that the volume ratio of the reagent to be injected and the sample solution could be fixed or controlled, without measuring the amount of the sample solution. Further, an optical characteristic was measured after further verifying that an

obstruction such as a bubble to the substantially parallel light 7 was eliminated after the inflow of the sample solution was suspended, and therefore, the measurement was highly reliable. Consequently, the measurement steps could be simplified, and furthermore, an erroneous operation was less likely to occur, resulting in an extremely high practicability, and higher efficiency and laborsaving of the measurement and the test became possible.

[0029]

<<Example 4>>

In the following, the method for controlling a measurement system and/or the method for measuring a concentration of a sample solution will be described.

Example 4 of the present invention will be described below in detail with reference to FIGS. 4 and 5. Herein, the explanation will be given for the case where the apparatus for measuring an optical characteristic shown in FIG. 4 was provided in a toilet bowl, and a protein concentration was examined by using a urine as a sample solution. In the apparatus for measuring an optical characteristic shown in FIG. 4, the solution surface 2, the semiconductor laser module 6, the substantially parallel light 7, the photosensor 8 and the computer 9 were the same as those in FIG. 1.

The sample cell 10 shown in FIG. 4 comprised a container made of aluminum which had the shape of a rectangular solid and a funnel-like opening 11 at the top of

its skeleton. Then, a glass plate as an optical window was embedded on both ends of the optical path, so that it allowed a light to be transmitted through the sample solution while holding the sample solution therein. The distance of the propagating direction of the light in the container, i.e., the distance between the optical windows was 10 mm, and the distance of a direction perpendicular to this propagating direction was 10 mm.

The optical axis of the substantially parallel light 7 was located at a height of 28 mm from the bottom of the sample cell 10. When the lowermost part of the surface 2 of the sample solution was located at the height two times the beam radius, from the optical axis of the substantially parallel light 7, that is, when the lowermost part of the solution surface 2 was located at a height of 30 mm from the bottom, approximately 99.97% of the total power propagated through the sample solution, as previously described. At this time, 3 ml of the sample solution was held in this sample cell 10.

[0030]

Further, an inlet 12 for injecting a reagent was located at the bottom of the sample cell 10, and a pipette 13, which injected a predetermined amount of the reagent into the sample solution in the sample cell 10 through the inlet 12, was controlled by the computer 9. Further, an elastic tube 14 for transferring the reagent connected the pipette 13 with the

inlet 12. A housing 15 is one made of resin, which integrated the semiconductor laser module 6, the photosensor 8, the sample cell 10, the inlet 12 and the tube 14 into one piece. The housing 15 had a sealed structure, and even when the sample solution splashed thereon, it did not reach the semiconductor laser module 6 and the photosensor 8, which were the optical components, and the optical windows on the outside of the skeleton of the sample cell 10.

[0031]

Next, FIG. 5 is a top plan view schematically showing the toilet bowl comprising the apparatus for measuring an optical characteristic shown in FIG. 4. The housing 15 was connected with a shaft base 17 via a cylindrical shaft 16. As shown in FIG. 5, the shaft base 17 was installed in a Western style toilet bowl 18. The shaft base 17 was controlled by the computer 9, and it moved the shaft 16 horizontally as indicated with the arrow to move the housing 15 into a bowl space 19 during the measurement of an optical characteristic of a discharged urine. Then, after the measurement was completed, it was restored underneath the toilet seat or the like, where it had been initially located. Herein, the tube 14 has been omitted from FIG. 5. In addition, it was possible to rotate the housing 15 in a direction parallel to the sheet of the paper in FIG. 4, that is, to rotate it about the shaft 16.

[0032]

The following is the operation for verifying an amount of a urine as a sample solution and further measuring a protein concentration thereof in this example.

First, according to instructions from the computer 9, the sample cell 10 was moved together with the housing 15 to the bowl space 19 of the toilet bowl 18, where the urine as the sample solution could be trapped easily. At this time, the test subject discharged a urine directly into the opening 11 of the sample cell 10. Herein, it was verified that the predetermined amount of the sample solution was held in the sample cell 10 based on the output signal S from the photosensor 8 by using any one of the methods shown in Examples 1 to 3. Upon the verification, the computer 9 gave instructions to restore, and the sample cell 10 was restored together with the housing 15 to the initial position.

[0033]

Next, the computer 9 controlled the pipette 13 to inject 3.0 ml of a sulfosalicylic acid reagent (a reagent obtained by dissolving sodium sulfate in an aqueous solution of 2-hydroxy-5-sulfobenzoic acid) into the sample cell 10. As a result, it was possible to mix the sample solution and the reagent at the ratio of 1:1. At this time, the computer 9 analyzed the output signal from the photosensor 8 to measure the concentration of the sample solution.

Subsequently, the computer 9 gave instructions, and the housing 15 was inclined by using the shaft 16 as an axis



to discharge the sample solution in the sample cell 10 into the toilet bowl 18 through the funnel-like opening at the top. Then, the sample cell 10, the opening 11, the housing 15 and the shaft 16 were washed. This washing was carried out, for example, by jetting a cleaning solution like a shower.

[0034]

As described above, according to this example, the amount of the sample solution held in the sample cell could be verified, so that the volume ratio of the reagent to be injected and the sample solution could be fixed or controlled, without measuring the amount of the sample solution. Further, the whole of the housing 15, which integrated the light source, the photosensor and the sample cell into one piece, was moved to the right place for trapping the sample solution, resulting in efficiency. An optical alignment error of the optical axis and the like was less likely to occur, as compared with the case where only the sample cell was moved at this step.

Moreover, since the housing 15 had a sealed structure, there was no danger that the sample solution and the like adhered to the respective optical components to obstruct the measurement.

In particular, when the sample solution was a urine, the sample cell 10 could be moved together with the housing 15 into the bowl space 19 of the toilet bowl 18 to trap a predetermined amount of the urine in the air. Consequently, the urine could be tested easily, and furthermore, an erroneous operation was less likely to occur and the

operational stability was improved, resulting in an extremely high practicability. That is, according to the present invention, higher efficiency and laborsaving of the measurement and the test became possible. Moreover, it was not necessary for the user to treat the urine directly, and therefore, the widespread use at home could be promoted.

[0035]

In this embodiment, the sample cell 10 was restored to the initial state in which it had been before it was moved into the bowl space 19, after verifying the amount of the sample solution, and an optical characteristic was measured thereafter; however, after the amount of the sample solution was verified, the sample cell 10 could be restored to the initial state in which it had been before it was moved into the bowl space 19, after the inflow of the sample solution was suspended to measure an optical characteristic.

Further, in this example, the sample cell 10 was washed after it was inclined to discharge the sample solution; however, the cleaning solution could be injected through the inlet 12 for the reagent while the sample solution was overflowed from the opening 11 without inclining the sample cell 10, thereby conducting the washing simultaneously. That is, the discharging and the washing might be carried out while replacing the sample solution with the cleaning solution.

[0036]

<<Example 5>>

In the following, Example 5 of the present invention will be described in detail with reference to FIGS. 5 and 6. In the apparatus for measuring an optical characteristic shown in FIG. 6, the solution surface 2, the semiconductor laser module 6, the substantially parallel light 7, the photosensor 8, the computer 9, the sample cell 10, the opening 11, the housing 15, the shaft 16 and the shaft base 17 were the same as those shown in FIG. 5 of Example 4. However, in this example, the substantially parallel light 7 was used only for verifying an amount of the sample solution, but not for measuring an optical characteristic of the solution. Also, the sample cell 10 was used as a container for trapping the sample solution, but not as a sample cell for holding the sample solution during the optical characteristic measurement.

In the apparatus for measuring an optical characteristic shown in FIG. 6, an electromagnetic valve 18 was controlled by the computer 9. A tube 19 transferred the sample solution trapped in the container 10 to another sample cell for measuring the characteristic. Also, as in Example 4, the housing 15 was connected with the shaft base 17 via the cylindrical shaft 16.

As shown in FIG. 5, the shaft base 17 was installed in a Western style toilet bowl 18. The shaft base 17 was controlled by the computer 9, and it moved the shaft 16 horizontally as indicated with the arrow to move the sample cell 10 together with the housing 15 into the bowl space 19

when measuring an optical characteristic of the discharged urine. Then, for example, after the measurement was completed, the sample cell 10 was restored underneath the toilet seat or the like, where it had been originally located. Also, it was possible to rotate the sample cell 10 together with the housing 15 in a direction parallel to the sheet of the paper in FIG. 4, that is, to rotate it about the shaft 16.

[0037]

The following is the operation for verifying an amount of a urine as a sample solution and further measuring a protein concentration thereof in this example.

First, according to instructions from the computer 9, the sample cell 10 was moved together with the housing 15 to the bowl space 19 in the toilet bowl 18, where the urine as the sample solution could be trapped easily. At this time, the test subject discharged the urine directly to the opening 11 of the sample cell 10. Here, it was verified that the predetermined amount of the sample solution was held in the container 10 based on the output signal S from the photosensor 8 by using any one of the methods shown in Examples 1 to 3.

At the time of the verification, the computer 9 gave instructions to the electromagnetic valve 18, thereby transfusing the sample solution to another sample cell for measuring the sample solution via the tube 19 for transferring. By conducting this transfusion on several separate occasions, concentrations of a plurality of specific substances could be

measured. That is, the sample solution was transfused to a sample cell first and a reagent was mixed therewith to measure the concentration of a certain specific substance, followed by discharging this sample solution. Subsequently, the sample solution was transfused from the sample cell 10 to the other sample cell again, and another reagent was mixed with the sample solution to measure a concentration of another specific substance.

[0038]

Upon completion of this series of measurements, the computer 9 gave instructions, and the housing 15 was inclined by using the shaft 16 as an axis to discharge the remaining sample solution in the sample cell 10 into the toilet bowl 18 through the funnel-like opening at the top. Then, the sample cell 10, the opening 11, the housing 15 and the shaft 16 were washed.

As described above, according to this example, a predetermined amount of the urine could be trapped in the air by the container moved into the bowl space of the toilet bowl. Then, it is possible to test the urine by transfusing the urine to the sample cell for holding the urine during the optical characteristic measurement of the urine. At this time, by conducting the transfusion on several separate occasions, a plurality of measurements could be conducted. Consequently, a plurality of test items could be examined easily, and furthermore, an erroneous operation was less likely to occur

and the operational stability was improved, resulting in an extremely high practicability. That is, according to the present invention, higher efficiency and laborsaving of the measurement and the test became possible. Moreover, it was not necessary for the user to treat the urine directly, and therefore, the widespread use at home could be promoted.

[0039]

<<Example 6>>

In the following, Example 6 will be described in detail with reference to FIGS. 7 to 9, in which a method for verifying an amount of a sample solution and a method for controlling a measurement system and/or a concentration of a sample solution of the present invention were used for measuring an optically active substance and a protein concentration in the sample solution.

FIG. 7 is a view showing the configuration of the apparatus for measuring an optical characteristic used in this example. Also, FIG. 8 is a top plan view schematically showing the apparatus for measuring an optical characteristic shown in FIG. 7.

In FIG. 7, the solution surface 2, the funnel 3, the electromagnetic valve 4, the pipette 5, the semiconductor laser module 6, the substantially parallel light 7, the photosensor 8 and the computer 9 were the same as those in the apparatus for measuring an optical characteristic shown in FIG. 1. A sample cell 19 was basically the same as the sample cell

1 of FIG. 1, but an optical window for introducing a scattered light, which arose when the substantially parallel light 7 propagated through the sample solution, to the outside of the sample cell was provided on the sidewall of the sample cell 19 in the direction of the short axis, that is, a direction perpendicular to the substantially parallel light 7 (not shown). In other words, as shown in FIG. 8, the optical window was provided such that a scattered light 26, which arose in the sample solution and propagated in the -y direction, could be detected by a photosensor 24.

[0040]

A polarizer 20 transmitted only a polarization component in the x direction in FIG. 7. Also, an analyzer 21 was arranged so as to transmit only a polarization component in the y direction shown in FIG. 8. In addition, by using an optical Faraday effect, an optical Faraday modulator 22 modulated and controlled the polarization direction, which was regulated in the x direction by the polarizer 20. A driver 23 controlled the optical Faraday modulator 22, and supplied a modulation signal to a lock-in amplifier 25, simultaneously. The photosensor 8 detected the substantially parallel light 7, which had been transmitted through the analyzer 21. The numeral 25 is a lock-in amplifier which performed a phase sensitive detection on the output signal from the photosensor 8 using the modulated signal of the optical Faraday modulator as a reference signal.

In this example, the computer 9 supplied a control current signal to the driver 23 so as to make the output signal from the lock-in amplifier 25 zero, thereby also playing a role in measuring an angle of rotation of the sample solution. In the case of this example, a modulation current having a frequency of 1.3 KHz was passed to the driver 23. By adjusting the modulation current, the modulation signal (control current signal or compensation control current), at which the output signal from the lock-in amplifier 25 was cancelled to become zero, was found to calculate the angle of rotation.

[0041]

The photosensor 24 for detecting the scattered light 26 measured the turbidity, when this output signal was analyzed by the computer 9 to opacify the sample solution by mixing thereto a reagent through the pipette 5. In general, the intensity of the scattered light 26, which arose in the sample solution before the mixing of the reagent, was extremely small and therefore was not detected by the photosensor 24.

~~...In this example also, as in Example 1, when the~~  
lowest part of the surface 2 of the sample solution was located at the height two times the beam radius, from the optical axis of the substantially parallel light 7, that is, when  $d = 10$  mm, approximately 99.97% of the total power propagated through the sample solution. At this time, 5 ml or



more of the sample solution of was held in the sample cell 19.

Herein, when the lowermost part of the solution surface 2 was located at a height of 8 mm from the bottom of the sample cell 1(sic), that is, when  $d = 8$  mm, only about a half of the total power propagated through the sample solution. When the solution surface 2 was located within the beam of the substantially parallel light 7 in this manner, the optical phenomena of reflection, refraction and diffraction concurrently occur on the solution surface, thereby diffusing the beam.

Then, the optical power that was sufficiently greater than the intensity of the scattered light, which had arisen in the sample solution before the mixing of the reagent, reached the photosensor 24, and this significantly fluctuated. Also, under the influence of the diffusion of the beam and the fluctuation of the solution surface, the optical power reaching the photosensor 24 did not stabilize. Moreover, as in Example 1, the optical power, which propagated through the analyzer 21 to reach the photosensor 8, was also influenced by the diffusion of the beam.

[0042]

FIG. 9 shows an example of the output signal S from the photosensor 24 when the sample solution was dropped into the sample cell 19 through the funnel 3 at 0.5 ml/sec in the apparatus for measuring an optical characteristic shown in FIGS. 7 and 8. In FIG. 9, the horizontal axis indicated the

distance  $d$  from the bottom of the sample cell 1(sic) to the lowermost part of the solution surface, and the vertical axis indicated the output signal  $S$  from the photosensor 24, whose maximum value was adjusted to be 1.0 V in the process of supplying the sample solution. Herein, in the sample cell 19 of this embodiment, when the sample solution was dropped at the above dropping rate,  $d$  became 1 mm one second after the dropping was started. Therefore, the horizontal axis of FIG. 9 also indicated the elapsed time since the start of the dropping of the sample solution. It should be noted that the sample solution was dropped into the sample cell 19 along the plane thereof without any optical window provided at three places of the sample cell, and therefore, the sample solution was not present in the optical paths of the substantially parallel light 7 and the scattered light 26 during the dropping.

As shown in FIG. 9, until  $d$  was approximately 6.0 mm, the output signal  $S$  was zero and no influence of the sample solution was observed; however, when  $d = 6.0$  to 10 mm, the output signal  $S$  significantly changed under the influence of the diffusion of the beam due to reflection, refraction or diffraction between the substantially parallel light 7 and the solution surface 2, and further the fluctuation of the solution surface. Then, when  $d$  was above 10 mm, it was apparently zero and stabilized.

[0043]

Based on such phenomena, any one of the methods of Examples 1 to 3 above might be used as the method for verifying an amount of a sample solution, but the method herein was set as follows.

First, with 5 ml or more of a sample solution being injected in the funnel 3 for trapping, the computer 9 sent an open signal to the electromagnetic valve 4, thereby starting the dropping of the sample solution in the funnel 3 into the sample cell 19 at 0.5 ml/sec. In the state of sending this open signal, the computer 9 was set to be in a state of being on standby for verifying an amount of a sample solution based on the fact that an absolute value of an amount of change in an output signal S from the photosensor 24 per hour  $dS(t)/dt$  had become the second predetermined value or greater. For example, the state of being on standby for verifying the amount of the sample solution was set when the absolute value of an amount of change in the output signal S per hour  $dS(t)/dt$  had become 0.1 V/sec or greater in FIG. 9.

In the state of being on standby for verifying the amount of the sample solution and sending the open signal, it was verified that a predetermined amount of the sample solution was held based on the fact that a state, in which the absolute value of the amount of change in the output signal S from the photosensor 24 per hour  $dS(t)/dt$  was the first predetermined value or less, had continued for the first predetermined time or longer. For example, it was verified

that the predetermined amount of the sample solution was held when a state, in which  $dS(t)/dt$  was 0.01 V/sec or less, had continued for 0.5 second or longer, and then a close signal was sent to the electromagnetic valve 4. By a control according to such a setting,  $d$  became 10.5 mm or greater and 5.25 ml or more of the sample solution was held in the sample cell 1(sic).

[0044]

The following is the operation for measuring a glucose concentration, i.e., a urine sugar value and a urine protein concentration using a urine as the sample solution in this state.

First, the computer 9 started to operate the driver 23 to measure an angle of rotation of the sample solution. Next, the computer 9 suspended the operation of the coil driver 23, and controlled the pipette 5 to drop a sulfosalicylic acid reagent (a reagent obtained by dissolving sodium sulfate in an aqueous solution of 2-hydroxy-5-sulfobenzoic acid) into the sample cell 19. In this state, the volume ratio of the sample solution and the reagent could be fixed or controlled by dropping the reagent. The protein concentration was measured by analyzing the change in the output signal from the photosensor 24 before and after the dropping of the reagent. With respect to this measurement of the protein concentration, the concentration was calculated in comparison with a calibration line that had been previously

prepared.

In the following, an example is shown, in which a urine having a urine sugar value of 100 (mg/dl) and a urine protein concentration of 15 (mg/dl) was measured as the sample solution.

[0045]

As a result of the measurement, the angle of rotation was approximately  $0.017^{\circ}$ . Herein, the specific angle of rotation of glucose at this wavelength (670 nm) was approximately  $40^{\circ}$  (deg/cm·dl/kg). Therefore, on the assumption that this angle of rotation was entirely due to glucose, the glucose concentration, i.e., the urine sugar value was 85 (mg/dl). Herein, the specific angle of rotation of protein was approximately  $-40^{\circ}$  (deg/cm·dl/kg). In other words, it was opposite in sign and the same in the absolute value, so that it was calculated at 85 (mg/dl) in the glucose concentration by subtracting 15 from 100, and therefore, it was confirmed that the measurement was carried out accurately.

When the protein concentration was measured by mixing the reagent and the output signal from the photosensor 24 was compared with the calibration line that had been previously prepared, the protein concentration was calculated at 15 (mg/dl), and therefore, it was confirmed that the measurement was carried out accurately.

[0046]

According to this example, since not only the amount

of change in the output signal  $S$  from the photosensor 24 per hour  $dS(t)/dt$ , but also the duration thereof was verified, the following erroneous operation could be prevented.

At a point of inflection, at which the output signal  $S$  from the photosensor 24 that had been decreasing turned to increase (or vice versa),  $dS(t)/dt$  reversed in sign of plus and minus. Therefore, at this point of inflection which appeared instantaneously,  $dS(t)/dt$  became zero. Thus, when it was verified only that an absolute value of  $dS(t)/dt$  had become the first predetermined value or less, an erroneous operation occurred. However, an erroneous operation due to such a plurality of points of inflection could be prevented by verifying not only the absolute value of the amount of change in the output signal  $S$  per hour  $dS(t)/dt$ , but also the duration thereof.

As described above, the amount of the sample solution could be verified during the inflow of the sample solution into the sample cell, by setting the state of being on standby for verifying the amount of the sample solution based on the fact that an amount of change in the output signal per hour  $dS(t)/dt$  had become the second predetermined value or greater and verifying that a predetermined amount of the sample solution was held when a state, in which  $dS(t)/dt$  was the first predetermined value or less, had continued for the first predetermined time or longer.

[0047]

In this example, since the substantially parallel light 7, which was a light for measuring an optical characteristic of the sample solution, and the photosensor 24 for detecting this were used for verifying the amount of the sample solution, it was not necessary to provide any means for verifying the amount of the sample solution separately. In other words, it utilized the original means for measuring an optical characteristic as the means for verifying the amount of the sample solution. Therefore, it was effective and highly practicable. However, it was obvious that the amount of the sample solution could be verified by providing another substantially parallel light and photosensor aside from the light for measuring an optical characteristic of the sample solution, and operating them in the same manner as in this example.

Further, according to this example, the amount of the sample solution held in the sample cell could be verified, so that the volume ratio of the reagent to be injected and the sample solution could be fixed or controlled, without measuring the amount of the sample solution. Consequently, the steps could be simplified, and furthermore, an erroneous operation was less likely to occur, resulting in an extremely high practicability. Also, higher efficiency and laborsaving of the measurement and the test became possible.

Further, according to this example, a protein concentration could be determined by measuring the angle of

rotation of the sample solution. That is, the protein concentration could be determined by measuring the angle of spontaneous rotation and the concentration of a spontaneous optically active substance based upon the angle of rotation due to a Faraday effect (magnetorotation) at which the angle of rotation due to the spontaneous optically active substance in the sample solution was identical with the angle of magnetorotation, and mixing a reagent therewith. This example was particularly practicable when the sample solution was a urine. As in this example, since the reagent was mixed with the sample solution after the measurement of the angle of rotation, both of them could be measured. The reason is that the mixing of the reagent might cause the protein component to coagulate or color, preventing a light from being transmitted through the sample solution. Additionally, the reagent might cause the protein to denature, thereby changing the angle of rotation thereof.

[0048]

Here, in this embodiment, the case was shown, in which the amount of the sample solution was verified based on the output signal S from the photosensor 24 for detecting a scattered light, but the output signal S from the photosensor 8 for measuring an angle of rotation could also be used. The substantially parallel light 7, which had been transmitted through the analyzer 21, was made incident on the photosensor 8; however, when the optical Faraday modulator 22 was not in



operation, the polarizer 20 and the analyzer 21 were arranged in a so-called crossed Nicol states, and therefore it was a leaked component that was transmitted through the analyzer 21, and therefore, it was significantly less as compared to the transmitted light component in Example 1 (approximately  $10^{-5}$  or less); however, it could be operated in the same manner as in Example 1 by adjusting S to be 1 (V) when  $d \geq 10$  mm.

Also, even when the optical Faraday modulator 22 was in operation, it could be operated in the same manner as in Example 1 by adjusting S to be 1 (V) when  $d \geq 10$  mm, so long as the rotating angle of the polarization direction was fixed.

It should be noted that the lights detected by the photosensor 24 included not only the scattered light that had arisen in the sample solution, but also the ones that had been reflected on the respective solution surfaces (the surface of a drop-like sample solution as well as the solution surface 2). Even on the assumption that the lights to be made incident on the photosensor 24 were only the reflected light components as above, the output signal from the photosensor 24 fluctuated greatly when the solution surface 2 was within the beam of the substantially parallel light 7, and the output signal from the photosensor 24 became stable when a predetermined amount of the sample solution was held, as shown in FIG. 9. Therefore, even if only the reflected light components were detected, the method of this example could be conducted. When the amount of the sample solution was verified in this manner, it was not

necessary to distinguish between these reflected light components and the scattered light components, and therefore, all of them were described as the scattered light 26 in this embodiment.

[0049]

<<Example 7>>

This example relates to the method for verifying an amount of a sample solution and the start of the measurement thereof by using the apparatus for measuring an optical characteristic shown in FIGS. 7 and 8 of Example 6 in the following manner. This example will be described with reference to FIGS. 9 and 10. FIG. 10 is an enlarged view of FIG. 9 showing the output signal S from the photosensor 24 at around 0 V, when  $d = 10$  to 12.

In this example, as in Example 6, with the sample solution being dropped into the sample cell 19, the amount of the sample solution was verified based on the fact that an amount of change in the output signal S from the photosensor 24 per hour  $dS(t)/dt$  was the second predetermined value or less and that the output signal S from the photosensor 4(sic) had become the fourth predetermined value or less. For example, it was verified that the predetermined amount of the sample solution was held when  $dS(t)/dt$  was 0.01 V/sec or less and S had become 0.01 V or less, and then a close signal was sent to the electromagnetic valve 4. By a control according to such a setting, d became 10 mm or greater, and therefore, 5

ml or more of the sample solution was held in the sample cell 19.

As such, according to this example, since the amount of the sample solution was verified based on not only the absolute value of the amount of change in the output signal S from the photosensor 24 per hour, but also the fact that the magnitude of the output signal S had become a predetermined value or less, the following erroneous operation that might occur in Example 6 could be prevented.

For example, when a bubble adhered to an optical window of the sample cell to be present in the optical path of the substantially parallel light 7 during the inflow of the sample solution into the sample cell, the substantially parallel light 7 was scattered and reflected by this bubble, and could not reach the photosensor 24. Even in this case, the absolute value of the amount of change in the output signal S from the photosensor 24 per hour might become 0.01 V/sec or less, resulting in an erroneous operation of mistakenly verifying that the predetermined amount of the sample solution was held. Such an erroneous operation due to a bubble, however, could be prevented by considering the magnitude of the output signal S for the judgment, in addition to the absolute value of the amount of change in the output signal S per hour.

[0050]

Next, from this state, it was verified that a state,

in which the amount of change in the output signal S per hour  $dS(t)/dt$  was the fifth predetermined value or less, continued for the second predetermined time or longer for starting the measurement of an optical characteristic of the sample solution. For example, the point of time, at which a state in which  $dS(t)/dt$  was 0.0015 (V/sec) or less had continued for 0.5 second or longer was verified. In FIGS. 9 and 10,  $dS(t)/dt$  had become 0.0015 (V/sec) or less when 11.1 seconds had elapsed, and therefore, it was verified when 11.6 seconds had elapsed.

When this was verified, an optical characteristic of the sample solution in the sample cell 19 was measured in the same manner as in Example 6.

[0051]

According to this example, since the amount of change in the output signal S from the photosensor 24 per hour  $dS(t)/dt$  and also the duration thereof were verified after verifying that the predetermined amount of the sample solution was held in the sample cell 19, the reliability of the measurement of an optical characteristic could be enhanced because of the following reason.

Even after the inflow of sample solution into the sample cell 19 was suspended, a bubble or the like generating during the inflow might be present in the optical path of the substantially parallel light 7, thereby causing a fluctuation in the output signal S from the photosensor 24. This

fluctuation deteriorated the reliability of the optical characteristic measurement. Therefore, the measurement was started after a bubble or the like disappeared from the optical path, for example, by surfacing, and the fluctuation in the output signal had subsided. In other words, the measurement was started after a state, in which the amount of change per hour  $dS(t)/dt$  was the fifth predetermined value or less, had continued for the second predetermined time or longer. Consequently, the reliability of the measurement could be ensured.

[0052]

As described above, according to this example, the amount of the sample solution held in the sample cell could be verified, so that the volume ratio of the reagent to be injected and the sample solution could be fixed or controlled, without measuring the amount of the sample solution. Furthermore, the measurement of an optical characteristic was carried out after further verifying that an obstruction due to a bubble or the like in the substantially parallel light 7 was eliminated after the inflow of the sample solution was suspended, and thus the measurement was highly reliable. Consequently, the steps could be simplified, and furthermore, an erroneous operation was less likely to occur, resulting in an extremely high practicability. Further, higher efficiency and laborsaving of the measurement and the test became possible.

[0053]

Hereinbelow, the above-described characteristics of the present invention will be described in detail.

When calculating the amount of change in the output signal  $S$  from the photosensor per hour  $dS(t)/dt$  in real time, it was necessary to either configure a differentiation circuit in an analog fashion or to perform a digital calculation. If the differentiation time constant of the circuit in the case of the analog differentiation circuit, or the sampling interval in the case of performing the digital calculation was not sufficiently less than the above first predetermined time or second predetermined time, the response speed would decrease to prolong the time required for verification of the predetermined amount of the sample solution after it was held. As a result, the time required for the entire measuring process was prolonged, resulting in reduced efficiency of the measurement. In each of Examples of the present invention, there was described the case where the differentiation time constant or the sampling interval was sufficiently less than the above first predetermined time and second predetermined time.

[0054]

#### [Effects of the Invention]

As described above, according to the present invention, the amount of the sample solution held in the sample cell can be verified, so that the volume ratio of the

reagent to be injected and the sample solution can be fixed or controlled without measuring the amount of the sample solution. Consequently, the steps can be simplified, and furthermore, an erroneous operation due to obstruction such as a bubble is less likely to occur, resulting in an extremely high practicability, and higher efficiency and laborsaving of the measurement and the test became possible.

Moreover, the whole of the housing 15, which integrates the light source, the photosensor and the sample cell into one piece, is moved to the right place for trapping the sample solution, resulting in efficiency. Unlike the case where only the sample cell is moved at this time, an optical alignment error of the optical axis or the like does not occur. Further, since the housing 15 has a sealed structure, there is no danger that the sample solution and the like adhere to the respective optical components to obstruct the measurement. In particular, when the sample solution is a urine, the whole of the housing 15 can be moved into the bowl space 19 of the toilet bowl 18 to trap a predetermined amount of the urine in the air. Consequently, the urine can be tested easily, and furthermore, an erroneous operation is less likely to occur and the operational stability can be improved, resulting in an extremely high practicability, and higher efficiency and laborsaving of the measurement and the test become possible. Further, it is not necessary for the user to treat the urine directly, so that the widespread use at home can be promoted.

[BRIEF EXPLANATION OF THE DRAWINGS]

[FIG. 1]

A view showing the configuration of the apparatus for measuring an optical characteristic used in Example 1 of the present invention.

[FIG. 2]

A graph showing the relation between the output signal from the photosensor and the distance from the bottom of the sample cell to the lowermost part of the solution surface or the elapsed time since the start of the dropping of the sample solution.

[FIG. 3]

An enlarged view of FIG. 2 showing the value of the output signal from the photosensor 8 at around 1.0 V, when  $d = 10$  to  $12$ .

[FIG. 4]

A view showing the configuration of the apparatus for measuring an optical characteristic used in Example 4 of the present invention.

[FIG. 5]

A top plan view schematically showing the toilet bowl comprising the apparatus for measuring an optical characteristic shown in FIG. 4.

[FIG. 6]

A view showing the configuration of the apparatus for measuring an optical characteristic used in Example 5 of the



present invention.

[FIG. 7]

A view showing the configuration of the apparatus for measuring an optical characteristic used in Examples 6 and 7 of the present invention.

[FIG. 8]

A top plan view schematically showing the apparatus for measuring an optical characteristic shown in FIG. 7.

[FIG. 9]

A graph showing the relation between the output signal from the photosensor and the distance from the bottom of the sample cell to the lowermost part of the solution surface or the elapsed time since the start of the dropping of the sample solution in Example 6 of the present invention.

[FIG. 10]

An enlarged view of FIG. 9 showing the value of the output signal S from the photosensor at around 0 V, when d = 10 to 12.

#### [Explanation of Reference Numerals]

1. Skeleton of sample cell
2. Solution surface
3. Funnel
4. Electromagnetic valve
5. Pipette
6. Semiconductor laser module
7. Substantially parallel light

8. Photosensor

9. Computer